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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/696,801	10/25/2000	Lee A. Bulla JR.	48279-3USPT	3203

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EXAMINER
CLOW, LORI A

ART UNIT	PAPER NUMBER
1631	22

DATE MAILED: 08/26/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Applicati n No.	Applicant(s)	
	09/696,801	BULLA ET AL.	
	Examiner	Art Unit	
	Lori A. Clow, Ph.D.	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 May 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *See Continuation Sheet* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13,14,16,17,19,23,25,26,34,36,38-41,45,47,48,60,61,64-66,70,72,73,81 and 82* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Continuation of Disposition of Claims: Claims pending in the application are 13,14,16,17,19,23,25,26,34,36,38-41,45,47,48,60,61,64-66,70,72,73,81 and 82.

DETAILED ACTION

Applicants' arguments, filed 22 May 2003, have been fully considered by they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claims 13, 14, 16, 17, 19, 23, 25, 26, 34, 36, 38-41, 45, 47, 48, 60, 61, 64-66, 70, 72, 73, 81, and 82 are currently pending.

Drawings

The drawing corrections filed 22 May 2003 are acknowledged.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 13, 14, 16, 17, 19, 23, 25, 26, 36, 38-41, 45, 47, 48, 60, 61, 64, 65, 66, 70, 72, 73, 81, and 82 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. *This is a new matter rejection.*

Claims 13 and 60 recite "prioritizing the extracted nucleotide sequences based on identity match and percent similarity with sequences having the highest identity match and highest percent similarity being highest priority." This is not supported in the specification as originally filed. The specification, beginning on page 29, lists numerous sequence comparison tools which include, for example, Gap, FrameAlign, and Overlap. However, not all alignment programs prioritize sequences in an alignment based on identity **and** percent similarity. For example, Overlap compares two sequences using a WordSearch style comparison (specification, page 32), FramAlign creates an optimal alignment of the best segment similarity (specification, page 30), and so forth. There is no basis in the specification that the steps of the instant invention should be practiced by prioritizing sequences according to **similarity and identity**. The originally filed claims do not include these limitations, thus the amendments to the claims are new matter.

Claims 14, 36, and 61 recite "which are regions commonly found in encoding nucleotide sequences." There is no support in the specification for this limitation. The specification simply discloses that filtering can be done by the numerous search programs listed (see page 16). The specification discloses removing artifactual sequences, for example, but does not recite regions found in **encoding** nucleotide sequences. The originally filed claims recite removing unwanted genes, which is entirely different from eliminating encoding nucleotide sequences. The amendments to the claims are new matter.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 13, 34, 60 and dependent claims are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 13, 34, 60 and claims dependent thereon recite "a method to design primers wherein said primers target a first nucleotide sequence which first nucleotide sequence results in at least one phenotypic characteristic." This is confusing in that the first nucleotide sequence would not result in a phenotypic characteristic. Rather, the claim would make more sense if it read, "wherein the expression of the first nucleotide sequence results in at least one phenotypic characteristic" or something to that effect.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 13, 14, 16, 17, 19, 23, 25, 26, 34, 36, 38-41, 45, 47, 48, 60, 61, 64-66, 70, 72, 73, 81, and 82 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 6,303,297 B1 (Lincoln et al.) in view of Rose et al. (Nucleic Acids Research (1998) Vol. 26, No. 7, pages 1628-1635).

US 6,303,297 B1 (from here on, '297) discloses a computerized storage and retrieval system for genetic information. Sequences are generated, edited, and annotated before entry into the internal database. Sequences are annotated and organized (prioritized) based upon their similarity to each other and to identified sequences (i.e. sequences available in public databases) (column 9, lines 36-38). Sequences are also edited to provide for more meaningful results by passing them through a series of screens that recognize unwanted sequence elements and removing those elements (see column 9, lines 63-67 and column 10). For example, repeat elements are eliminated that may have a high identity with another sequence. Edited sequences are then analyzed against a basic informative database, such as GenPept. Matches receive a BLAST score that indicate the quality of the alignment between matched sequences. If no significant matches are found in GenPept, the sequence is compared against GenBank Primate

database or GenBank Rodent database (column 12, lines 38-65). Following the screening procedures, sequences with a significant amount of identity are organized into a linkage cluster using a pair-wise alignment analysis (see details column 13, beginning line 5). The database is organized such that users may access information pertinent to DNA sequences. Both sequences and annotations are stored in the relational database and users access the information via an integrated network consisting typically of computers that have output devices, display, memory, and interface to the network (column 15, lines 40-59).

Sequences and associated annotations are stored in an expression database. The annotations may contain information on the cells and tissues where the genes corresponding to the isolated cDNA sequences are expressed, identity to known genes, probable gene product function, and preparation techniques (column 16, lines 6-12). One important aspect of the invention is that the expression profiles of potential test sequences can be related to expression profiles of known sequences (column 18, lines 32-42). The database may be used for many types of analysis both within the internal database and between sequences in the internal database and those in publicly available databases (column 19, lines 20-24). These database functions provide information on homology, functional motifs or domains, and protein patterns of the compared sequences that may be predictive of activity (column 19, lines 51-54). Finally the example at column 24, lines 16-42 describe the use of this database for gene discovery.

While '297 does not teach the primer design method per se, the suggestion to use this database for many applications is apparent (see again column 19, lines 20-24). Rose et al. do teach a primer design strategy for PCR amplification of unknown targets that are related to multiply-aligned protein sequences. This program is capable of isolating homologous sequences

from multi-gene families. It is acknowledged in the art that isolation of unknown sequences related to known sequences is a powerful method for investigating biological function. This method bases primer design on precisely-matched regions only and is therefore more sensitive than consensus and degenerate primer design (see discussion). In the examples (page 1633, column 1) internal (nested) primers are used.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to combine the primer design system of Rose et al. with the relational database of '297. One would have been motivated to do so because'297 states that this database can be useful for a variety of biological assays, including identification of genes that may be used to subsequently aid in the identification of tissues of a sample of unknown derivation or novel genes specific to a selected cell type. Furthermore, specific match sequences can be chosen based upon similarities or differences in the samples used to generate sequences (column 23). The CODEHOP method of Rose et al. is available on the World Wide Web for interactive use. The multiple alignments generated by the relational database based upon annotations representing phenotypic data of '297 could easily be used for data alignments in the CODEHOP primer design system. While neither of the methods provide for the specific phenotype of expression in insect mid-gut epithelium, it would be obvious to use these systems to analyze a wide variety of phenotypic characteristics where the motivation is provided by Lincoln's teaching that databases of this sort are designed for identification of homologues for **any** gene, in general (Lincoln et al., see abstract; see column 19, lines 51-54).

No claims are allowed.

Inquiries

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located

in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR § 1.6(d)). The CM1 Fax Center number is either (703) 308-4242, or (703) 308-4028.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lori A. Clow, Ph.D., whose telephone number is (703) 306-5439. The examiner can normally be reached on Monday-Friday from 10am to 6:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael P. Woodward, Ph.D., can be reached on (703) 308-4028.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Legal Instrument Examiner, Tina Plunkett, whose telephone number is (703) 305-3524, or to the Technical Center receptionist whose telephone number is (703) 308-0196.

MARJORIE MORAN
PATENT EXAMINER

August 21, 2003
Lori A. Clow, Ph.D.
Art Unit 1631